

the double patenting rejection, rather than attempt a terminal disclaimer, the Applicant has deleted the existing claims 1-7 on file and presented distinguished newly drafted claims 8-17 for the Examiner's kind consideration. It is noted that the applicant wishes to reserve the right of pursuing the subject matter of the deleted claims 1-7 later, by way of a divisional application if need be. It is believed that with the deletion of the claims 1-7 presently on file, the double patenting rejection issue regarding the claims 1-7 is resolved.

The newly presented independent claims 8, 11, and 13 are directed respectively to "A method of potentiating action of anti-angiogenic substances.....", "A method of selectively inhibiting endothelial cell proliferation and causing necrosis of tumor-cells..." and "A method of treating mammalian cell proliferative disorder including Hodgkin's disease...", and are believed not to give rise to any double patenting situation based on the cited earlier US patent 6,380,253 B1 to Das.

**Support in the text as originally filed, for the newly presented claims 8-17:**

1. New claim 8 is directed to a method of potentiating anti-angiogenic substances by the use of PUFAs and is supported at least by the invention-title and paragraphs 31 and 43 of the text as originally filed. The step of "administering" in claim 8 is supported at least by the subject matter of paragraphs 55 and 56, as originally filed.
2. New claim 9 depends from claim 8 and is supported additionally by at least paragraph 32 of the text as originally filed.
3. New claim 10 depends from claim 8 and is supported by at least paragraph 31 of the text for the lymphographic agent.
4. New claim 11 is independent and is supported by at least paragraphs 30, 32 and 35 of the text as originally filed. The step of "administering" in claim 11 is supported at least by the subject matter of paragraphs 55 and 56, as originally filed. The method step of

inhibiting endothelial cell proliferation is supported at least by the subject matter contained in paragraph 30 of the text as originally filed.

5. New claim 12 is dependent from claim 11 and is supported by at least by the subject matter of paragraph 32 of the text as originally filed.

6. New claim 13 is directed to treating Hodgkin's disease and is supported at least by the subject matter disclosed in paragraphs 42 and 43 as originally filed.

7. New claim 14 recites Angiostatin and Endostatin, and is supported similar to claim 11, by at least paragraphs 32 and 35 of the text as originally filed. The step of oral administration of the emulsion in claim 14 is supported at least by the subject matter contained in paragraph 43, and 56 as originally filed.

8. New claim 15 depends from claim 13, and is supported at least by the subject matter contained in paragraph 39 as originally filed.

9. New claims 16 and 17 depend from claim 15 and are additionally supported at least by the subject matter contained in paragraphs 40, 41, 42 and 43 as originally filed.

A favorable consideration of the newly presented claims 8-17 is earnestly requested. It is believed that no additional fee is due at this time.

If the Examiner considers that a telephone conversation with the undersigned would be conducive to making progress towards completing prosecution of the case, the undersigned may be reached at 215 6651 1140 during EST office hours.

Respectfully submitted,

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**Marked up claims for US Serial Number 10/083,529**

**1. (Deleted, previously wrongly labeled as claim 2)** A method of inhibiting blood supply to a tumor, comprising the steps of:

- (a) locating an artery which carries major blood supply to the tumor, said artery being one that is proximate to the tumor;  
and
- (b) intra-arterially injecting into the located artery a predetermined quantity of one or more anti-angiogenic substance(s), and a salt of at least one polyunsaturated fatty acid chosen from linolenic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid and cis-parinaric acid.

**2. (Deleted)** A method as in claim 1 comprising the step of causing antiangiogenic action, wherein said polyunsaturated fatty acid is in the form of a lithium salt solution and wherein said predetermined quantity of the fatty acid is generally in a range of 0.5 mg to 50 gm.

**3. (Deleted)** A method as in claim 1 wherein step (b) comprises intra-arterially injecting said predetermined quantity of a polyunsaturated fatty acid in the form of a lithium salt solution of a polyunsaturated fatty acid, wherein said anti-angiogenic substance is to the extent of 1 to 1000 mg/kg/ body weight, said solution of polyunsaturated fatty acid further comprising a substance chosen from glycerides, esters, free acids, amides, phospholipids and salts.

**4. ( Deleted)** A method as in claim 1, wherein the polyunsaturated fatty acid is

in the form of a lithium salt solution of gamma-linolenic acid and eicosapentaenoic acid/docosahexaenoic acid, including a predetermined quantity of said anti-angiogenic substance chosen from: an anti-angiogenic substance naturally occurring as a protein, platelet factor-4, TNP-470, thalidomide, interleukin-12, and metalloprotease inhibitors, and a predetermined anti-cancer drug.

**5. (Deleted)** A method of treating a tumor and facilitating visualization of remission of the tumor responsive to treatment, comprising :

- (a) locating an artery which carries a major portion of blood supply to said tumor and is adjacent to the tumor;
- (b) obtaining an initial radiographic image of the tumor region;
- (c) injecting into the located artery a mixture of at least
  - (i) an oily lymphographic agent as a carrier containing one or more of anti-angiogenic substance(s)
  - (ii) a lithium salt solution of at least one polyunsaturated fatty acid chosen from linolenic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid,

eicosapentaenoic acid, docosahexaenoic acid and cis-parinaric acid.

(d) obtaining second and subsequent radiographic images of the tumor region after predetermined lapses of time; and

(e) comparing the initial radiographic image with the second and subsequent images to assess an extent of remission of the tumor.

**6. (Deleted)** A method as in claim 5 wherein step (c) comprises intra-arterially injecting said mixture containing components chosen from: an anti-angiogenic substance naturally as a protein, platelet factor-4, TNP-470, thalidomide, and interleukin-12, causing anti-angiogenic action by inhibiting the blood supply to the tumor, wherein further the oily lymphographic agent acts as a carrier for said anti-angiogenic substance(s), and also for the lithium salt solution of predetermined quantities of gamma-linolenic acid, eicosapentaenoic acid and/or docosahexaenoic acid.

**7. (Deleted)** A method of treating a cancerous tumor, comprising

(a) using an oily lymphographic agent as a carrier for

(i) at least one polyunsaturated fatty acid chosen from a lithium salt of at least one of linolenic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic

acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid, and cis-parinaric acid; and,

(ii) a predetermined anti-cancer drug, and anti-angiogenic substance(s) mixed with polyunsaturated fatty acids or coupled with fatty acids; and,

(b) administering, by injecting into said cancerous tumor a predetermined quantity of the fatty acids, anti-cancer drug and predetermined anti-angiogenic substance in the oily lymphographic agent as a carrier.

**New Claims for US serial No. 10/083,529, Dr Das, Div 1**

**8. (new)** A method of potentiating anti-angiogenic substances by the use of Poly Unsaturated Fatty Acids (PUFAs) for treating hepatocellular carcinoma, comprising:

using a combination of selected PUFA/PUFAs and a lithium salt with an anti-angiogenic substance; and,

administering said combination by one or different routes selected from a group consisting of oral, parenteral, intravenous, subcutaneous, intra-peritoneal, topical, anal, vaginal and local injection.

**9. (new)** The method as in claim 8 wherein said anti-angiogenic substance is selected from ANGIOSTATIN and ENDOSTATIN, and said selected PUFA is chosen from a group consisting of: linolenic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid and cis-parinaric acid.

**10. (new)** The method as in claim 8 including using a lymphographic agent with said PUFAs.

**11. (new)** A method of selectively inhibiting endothelial cell proliferation and causing necrosis of tumor-cells by delivering a selected combination of Poly Unsaturated Fatty Acid (PUFA) in conjugation with a lithium salt, a lymphographic agent and an anti-angiogenic substance chosen from ANGIOSTATIN and ENDOSTATIN, the method including the step of administering said combination by one or different routes chosen from a group consisting of oral, parenteral, intravenous, subcutaneous, intra-peritoneal, topical, anal, vaginal and local injection.

**12. (new)** The method as in claim 11, wherein said PUFA comprises one or more PUFAs selected from a group consisting of linolenic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid and cis-parinaric acid.

**13. (new)** A method of treating mammalian cell proliferative disorder including Hodgkin's disease, comprising the steps of:  
using an emulsion of a lithium salt of a Poly Unsaturated Fatty Acid chosen from linolenic acid, gamma-linolenic acid, dihomo-gamma-linolenic acid, arachidonic acid, alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid and cis-parinaric acid,  
and,  
an anti-angiogenic protein/peptide substance.

**14. (new)** The method as in claim 13, wherein the anti-angiogenic substance is chosen from ANGIOSTATIN and ENDOSTATIN, said method including the step of administering said emulsion and the anti-angiogenic substance orally.

**15. (new)** The method as in claim 13, including the step of additionally using lymphokines and anti-cancer drugs, for treating said mammalian cell proliferative disorder.

**16. (new)** The method as in claim 15, wherein the lymphokines include TNF (Tumor Necrosis Factor) and IFN (Interferon).

**17. (new)** The method as in claim 15, wherein said anticancer drugs selectively comprise Doxorubicin and Vincristine.